Studies on Therapeutic Effect of Solcoseryl on Leucopenia induced by Co^{60} or X ray irradiation

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Co^{60} および X 線照射による白血球減少に対する Solcoseryl の治療研究

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Co^{60} およびX線照射による白血球減少症に対して，防禦および治療効果を示す Marinamycin (1957) の対照として，gaeger の Solcoseryl (造器製剤) により，家兎を用いて，白血球減少症に対する試験を行つた．

1) 正常家兎に Solcoseryl の少量を静脈内に注射すると，6000—10000 の増加を示すが投与量が多いとむしろ，減少を示すことが認められた．

2) 家兎の静脈内に Solcoseryl 20mg(製品 0.5 ml) を注射した後，2時間後 Co^{60} 又は X線照射を行う，即ち前投与によつて，この範囲の実験では白血球減少を防禦することは出来なかつた．

かゝる家兎に Marinamycin 2.0mg を1回だけ投与すると，速かに快復することが認められた．

3) Co^{60} 300γ を全身照射した後，Solcoseryl の少量を毎日投与すると，約2週間で，快復することが認められた．

Introduction

Prophylatic and therapeutic effect of Marinamycin[1)2)3)4)] an antibiotic substance, on leucopenia induced by X-ray or Co^{60} irradiation or by administration of anti-cancer agents has been reported by Soeda et al. since 1957. Other substances such as adnine sulfate, benzyl Kinetin (Okumura) and Aloetin[6)] (Soeda) have been studied in parallel with Marinamycin as controls, and it gradually became clear that the nature of their effects to enhance WBC count of peripheral blood are apparently different from that of Marinamycin. Thus, repeated administrations of these agents are required for appearance of their beneficial effects on WBC counts.

The purpose of this paper is to describe several interesting findings obtained from studies on leucocytotic effect of Solcoseryl,[7)8)] an organ-preparation found by Jeager, in contrast with Marinamycin.

Experimental Materials and Method

1. Solcoseryl used for studies was obtained by courtesy of Tobishi Co. in forms of 2 ml. ampules, which contain 40 mg Solcoseryl per ml.
2. Male rabbits weighing about 2.5 Kg were employed as experimental animals.
3. X ray irradiation of rabbits was conducted by Dr. Oide, Division of Radiological Therapy,

Central Hospital, J.D.A., and Co^{60} irradiation of animals was done by Drs. Urai and Yuhara, V. Division of Ist. Research Center, Technical Research and Development H.Q., J.D.A., Tokyo.

4. Solcoseryl was administered to rabbits by the intravenous route in all experiments.

5. White cell count was performed according to the ordinary methode. Peripheral blood samples were taken from auricular veins of rabbits with tuberculin syringes and 1/3 or 1/4 gauge needles and ten times diluted with zuerk solution. Cell countings were performed ten times per one blood sample and the average value was regarded as its WBC reading.

6. General irradiation of rabbits by Co^{60} was done as follows: Each rabbit was placed in a separate case set around the source of Co^{60} with a power of 300r. Each cage was maintained at the same distance from Co^{60} source 57cm) and several dosimetric instruments were employed to obtain exact radiation doses.

Experimental Results

Experiment 1)

A daily dose of 20 mg of Solcoseryl was intravenously injected to rabbit (No. 75, weighing 2.8 Kg) three times at intervals of 3 to 5 days (Fig. 1). Another rabbit weighing 3.0 Kg was intravenously given 80 mg Solcoseryl on the initial day and additional two doses of 20 mg Solcoseryl at intervals of 3 to 5 days (Fig. 2). As shown in Fig. 2, a too much dose of this agent seemed to cause a temporal leucopenia in rabbits.

Experiment 2)

Prophylactic and therapeutic effect of Solcoseryl on leucopenia induced by general exposure of animals to 300r (Co^{60}) was tested in this experiment. A dose of 20 mg of Solcoseryl was interavenously given to a rabbit (No. 75, weighing 2.8 Kg) two hours prior to irradiation. As previously reported, almost the same experiment had been carried out with Marinamycin, in which only 2.0 mg of this agent was demonstrated to be sufficient to prevent the occurrance of leucopenia in animals generally exposed to 300r. But such effect was absent in Solcoseryl and a significant leucopenia occurred immediately after irradiation. Making a start on the 14th. day, adose of 10 to 40 mg of Solcoseryl was intrvenously given to the same rabbit 4 times at intervals of 1 to 3 days. (Fig 3)

Fig. 1 The effect of Solcoseryl on the white-cell count of a control rabbit (No. 75, weighing 2.8 kg.)

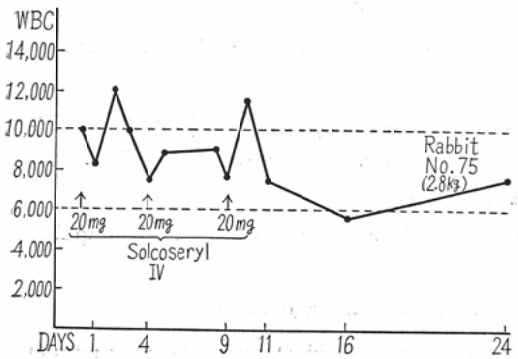
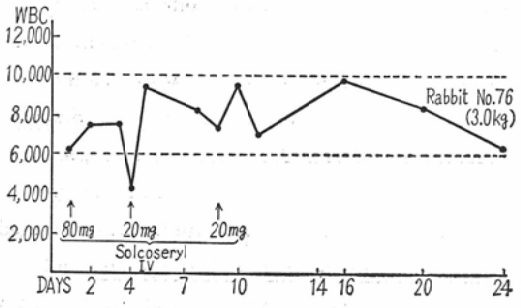


Fig. 2 The effect of Solcoseryl on the white-cell count of another control rabbit (No. 76, weighing 3.0 kg.)



Another rabbit (No. 76, weighihg 3.0 Kg) was given 20 mg Solcoseryl two hours prior to exposure and again 20 mg of this agent on the next day. Beggining on the 14th. day, a dose ranging from 10 to 40 mg was intravenously given 3 times at variable intervals (Fig. 4). Except for temporal elevation of WBC count, medication of Solcoseryl appeared to have almost no special prophylactic or therapeutic effect so far as white-cell count is concerned.

Experiment 3)

A dose of 10 mg of Solcoseryl was intravenously given to a rabbit (No. 82, body wt. 2.9 Kg) two hours before general exposure to 300 r (Co^{60}) and beggining on the 3rd. day, the same dose was repeatedly injected 8 times during the course of 10 days. Another rabbit (No. 81, body wt. 2.8 Kg) was treated in the same manner before exposure, and beginning on the 3rd. day, a dose of 20 mg was repeatedly given 8 times within 9 days. (Fig. 5 and 6.)

As seen in Fig. 5 and 6 although a single or a few doses of 10 to 20 mg of Solcoseryl seem to be

Fig. 3 Prophylactic and therapeutic effect of Solcoseryl on leucopenia induce by general exposure of a rabbit to 300 r of Cobalt-60. (a daily dose: 4 to 40 mg.)

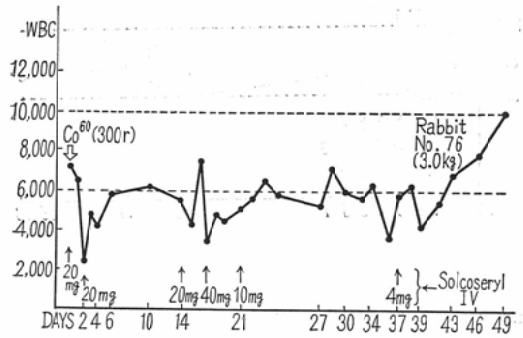


Fig. 4 Prophylactic and therapeutic effect of repeatedly administered Solcoseryl on leucopenia induced by general exposure of another rabbit to 300r of Cobalt-60. (a daily dose: 10 to 40 mg.)

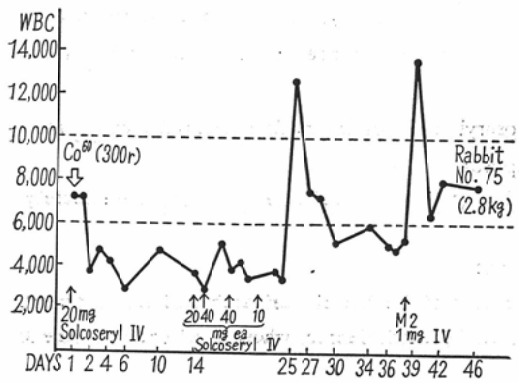


Fig. 5 The effect of Solcoseryl repeatedly given at short intervals on leucopenia in rabbits induced by general exposure to 300r of Cobalt-60. (a daily dose: 10 mg.)

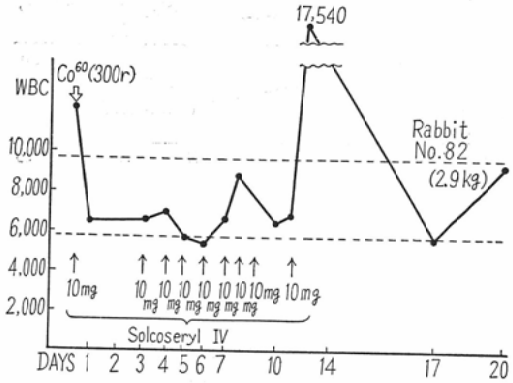
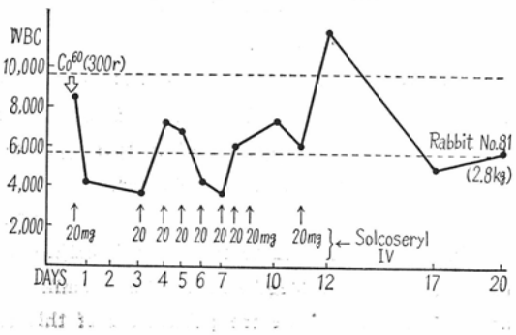


Fig. 6 The effect of Solcoseryl repeatedly given at short intervals on leucopenia in rabbits induced by general exposure to 300r of Cobalt-60. (a daily dose: 20 mg.)



almost of no effect on leucopenia in irradiated rabbits, repeated medications at short intervals appear to be significantly beneficial for restoration of WBC count in peripheral blood.

Experiment 4)

A daily dose of 10mg of Solcoseryl was intravenously given to two rabbits (No. 87, and No. 88) for 4 successive days, 24 hours after general exposure to 300r (Co^{60}). As shown in Fig. 7, WBC count rapidly increased shortly after the medication was over, and WBC count more than 6,000 was maintained throughout the course of observation.

Experiment 5)

A daily dose of 10 mg of Solcoseryl was intravenously given to a rabbit (No. 89, body wt. 2.8 Kg) for 6 successive days, 24 hours after X ray irradiation (300r). The results are shown in Fig. 8.

Fig. 7 The effect of Solcoseryl on induced leucopenia in rabbits by general exposure to 300r of Cobalt-60, when a daily dose of 10 mg. was intravenously given for 4 succesive days after exposure.

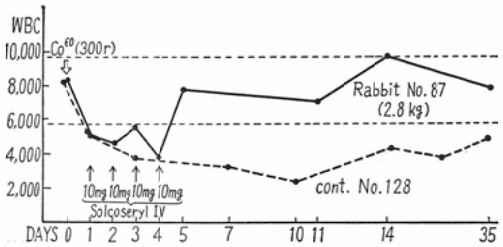
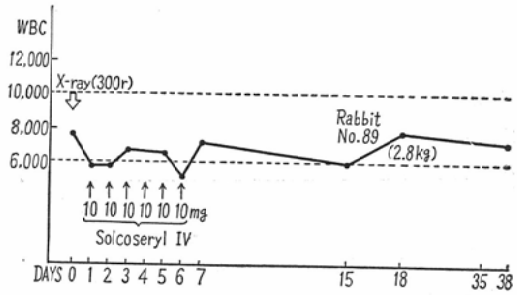


Fig. 8 The effect of Solcoseryl on induced leucopenia in rabbits by general irradiation with 300r of X-ray, when a daily dose of 10 mg. was intravenously given for six succesive days after irradiation



Conclusions

1) When a smaller dose of Solcoseryl was intrvenously injected to normal rabbits several times at intervals of 3 to 5 days, white cell count of peripheral blood remained almost unchanged within the range of 6.000 to 10.000, and we did not find any significant leucocytosis or leucopenia after mediaction. A larger dose, however, appeared to cause a temporal drop in white-cell count of short duration.

2) A single medication of 20mg Solcoseryl could not prevent the occurrance of leucopenia in rabbits generally exposed to 300 r by Co^{60} or X ray irradiation. On the contrary, only 2.0 mg Marinamycin had been demonstrated to be sufficient to protect animals from occurrance of leucopenia induced by such radiation dose.

3) Repeated medication of a smaller dose of Solcoseryl at short intervals appeared significantly beneficial for recovery from induced leucopenia by exposure to 300r.

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Acknowledgment

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